Cost-Effectiveness Analysis in HIV Prevention Planning: A Guide to Understanding the Literature

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Section I. Introduction

This document is a basic guide to the economic evaluation literature on HIV prevention. It is not meant to provide a comprehensive review of this literature. Instead, the main purpose is to make this literature more accessible—by familiarizing readers with various potential uses of economic analyses and the techniques and terminology employed in the literature—and in the process, to help "demystify" cost-effectiveness analysis and related economic evaluation techniques. The larger goal is to assist HIV prevention community planning groups in complying with the *CDC Guidance on Community Planning*, which asks that community planning groups consider the cost-effectiveness of HIV prevention interventions when making decisions about priorities.

The primary audience for this guide are the grantees of CDC-funded cooperative agreements developing practical approaches to the use of cost-effectiveness in HIV prevention, including: the Academy for Educational Development (AED), Emory University, Medical College of Wisconsin-Center for AIDS Intervention Research (MCW-CAIR), RAND Corporation, Research Triangle Institute (RTI), and University of California-San Francisco Center for AIDS Prevention Studies (UCSF-CAPS). This document provides a common foundation for understanding the literature, illustrates the breadth of this literature, and establishes a shared vocabulary to support project partners' products. The secondary audience includes CDC Project Officers, health departments, community planning groups, and the greater HIV prevention community.

This literature guide consists of two main sections. The first section identifies several categories of potential applications of **economic evaluation** techniques. Each category is defined and illustrated using one or more examples from the literature. Application categories include:

- *Resource advocacy:* used to document that allocating more resources to HIV prevention can be a good investment and can save money over the long term by averting expensive HIV/AIDS-related medical care costs.

- *Policy advocacy:* used to support specific public health policy objectives by demonstrating that particular intervention strategies (e.g., needle exchange programs) could be **cost-saving** or cost-effective if funding were increased.

- *Targeting prevention efforts:* used to demonstrate the increased cost-effectiveness achieved by focusing HIV prevention resources on specific, high-risk populations.

- *Intervention evaluation:* used to assess whether or not a particular intervention is cost-effective relative to alternatives.

- *Intervention comparisons:* used to compare the cost-effectiveness of different interventions.

- *Intervention prioritization:* used to provide guidance in comparing different interventions targeted to the same target population for the purpose of setting priorities.

- *Resource allocation:* used to provide guidance on how available HIV prevention resources could be allocated to different programs in order to achieve a specified objective, such as preventing as many HIV infections as possible.

The second section of this document defines and discusses standard **economic evaluation** concepts in relatively simple, accessible language. This discussion focuses on application of cost-effectiveness analysis and related techniques to HIV prevention. Examples and a brief overview of relevant modeling methods are also provided.

A selected bibliography of relevant books, articles, and book chapters is provided at the end of this document.

Section II. Illustrative Applications from the Literature

The HIV prevention economic evaluation literature supports a variety of uses, from establishing that a particular intervention or HIV prevention strategy is (or is not) cost-effective, to demonstrating the need for increased HIV prevention funding or better targeting of existing economic resources. There is, of course, considerable overlap between categories. Some of these various uses are described and illustrated below. The discussion presented here is not intended to provide a comprehensive overview of these topic areas—only to give the reader an idea of the diverse uses of HIV prevention economic analyses. (Terms in bold are described in the glossary.)

Resource Advocacy

Studies in this category attempt to address the very difficult question of whether the U.S. is spending too little or too much on HIV prevention. Although some people might argue that the more-or-less steady rate of new infections over the past decade (approximately 40,000 per year) indicates that HIV prevention is underfunded, economic resources are by nature limited, and there are many other significant health issues and pressing social concerns competing for funding with HIV prevention. Economic analyses of the cost of providing HIV prevention services to at-risk populations, and the potential impact of these services, can assist public health decision makers in the arduous task of determining whether HIV prevention funding should be increased or reduced.

Holtgrave and colleagues (2002) estimated the cost of addressing unmet HIV prevention needs in the U.S., and conducted a **threshold analysis** to determine the number of new infections that would need to be averted in order for such a national HIV prevention initiative to be **cost-saving**. They included several interventions in their analysis: HIV counseling and testing; sex risk reduction programs; interventions to increase injection drug users' access to sterile syringes; and intensive programs for HIV-seropositive persons to help them avoid transmitting the virus to others. The estimated cost of providing this comprehensive array of prevention services to 5 million high-risk persons in the U.S. ranged from $817 million to $1.85 billion, depending upon the intensity of the interventions offered. To offset this cost through future savings in averted HIV/AIDS-related medical care costs would require preventing 5300 to 12,000 new infections, respectively. The authors note that the same type of **threshold analysis** can be applied to the CDC's stated goal of reducing new infections to 20,000 per year by 2005. Taking into account the future savings in medical care costs that would result from such a reduction, Holtgrave and colleagues suggest that society should be willing to spend up to $3 billion to achieve this goal. This is many times over the current national HIV prevention budget.

Policy Advocacy

Economic evaluation can serve an important policy advocacy function by demonstrating that by not funding (or underfunding) a particular HIV prevention strategy, lives are being lost, health is being compromised, and money is being wasted. For example, Chesson and Pinkerton (1999) estimated that, in 1996, there were 1082 new HIV infections among heterosexuals that could be attributed to syphilis' facilitative effect on HIV transmission. These infections were associated with $211 million in future HIV-related medical care costs and $541 million in indirect costs (including economic productivity losses); these future costs are substantially greater than the estimated cost of the CDC's plan to eliminate syphilis. Thus, by spending money now (and in the next several years) to reduce the incidence of syphilis in the U.S., a net savings—due to prevented HIV infections—could be achieved in the years ahead. By demonstrating a favorable "bottom line," this type of analysis can be helpful for advocating for a particular intervention strategy. From an advocacy standpoint, the results are most persuasive when they indicate that a program is **cost-saving** (i.e., it pays for itself even as it saves lives and improves the nation's health).

Even without program cost estimates to establish that an intervention is **cost-saving**, analyses that estimate the number of HIV infections that *could* have been averted, and the dollars that *could* have been saved, had an intervention been implemented, can be compelling advocacy tools. For example, Lurie and Drucker (1997) used a simple mathematical model to estimate the number of infections that needle exchange programs could have averted had they been in place early in the epidemic (from 1987 to 1995). The model included infections among injection drug users, their sex partners, and their children. Assuming a 15% to 33% reduction in HIV incidence as a consequence of needle exchange, they estimated that between 4394 and 9666 infections could have been averted, saving between $244 million and $538 million in HIV/AIDS medical care costs. Although the exact cost of reaching the targeted reductions in incidence is not known, the cost saving estimates reported by Lurie and Drucker suggest that substantial funding could be allocated to needle exchange programs without exceeding the savings these programs would generate. The authors therefore concluded that, "Revoking the U.S. government ban on funding for needle-exchange programs and accelerating the growth of such programs in the USA are urgent public health priorities."

Targeting Prevention Efforts

To maximize the public health impact of spending on HIV prevention, interventions must be appropriately targeted. HIV prevention resources are limited. Expending resources on very low risk persons—who, by definition, are very unlikely to become infected—diverts funds away from higher-risk populations where the impact of spending on HIV prevention programs is greater. Cost-effectiveness models can be used to quantitatively address the targeting issue and to suggest qualitative guidelines for maximizing the national investment on HIV prevention.

Kahn (1996) developed a mathematical model to examine the impact and cost-effectiveness of HIV prevention interventions when implemented in hypothetical populations of various risk levels, as quantified by the prevalence and incidence of infection, and the stage of the epidemic (steady-state, pre-steady-state, or post-steady-state). The results of his analysis of targeting prevention resources to different populations were quite dramatic. Spending an additional $1 million to fund interventions for a high-risk, steady-state population would prevent 164 infections over a 10-year period. This same funding level would prevent only 0.4 infections in a very-low-risk population over the same period of time and the same number of people served.

Based on this analysis, Kahn concluded that, “Targeting appears to provide substantial benefit and should be considered in allocation decisions about prevention.” This does not mean that lower-risk populations should be neglected, only that HIV prevention efforts should be directed toward high-risk populations *first*.

Intervention Evaluation

There is a growing literature on the cost-effectiveness of specific HIV prevention interventions. The goal of these studies is to estimate the cost-effectiveness of a particular intervention, as implemented in a particular population. Cost-effectiveness ratios have been estimated for a range of intervention types, including counseling and testing programs, condom distribution, small-group counseling, community-level (norm change) interventions, programs to increase access to sterile syringes (including needle exchange), drug abuse treatment/methadone maintenance as HIV prevention, post-exposure prophylaxis with antiretroviral agents, and programs that combine two or more of these prevention strategies. These interventions serve various populations, including men who have sex with men, other at-risk men, at-risk women, injection drug users, school-age children, young adults, and the so-called general population. The estimates reported in these studies can inform the community planning process by providing evidence that a particular intervention is or is not cost-effective for a particular population group, and can be used by decision makers in the **resource allocation** process (see the “Intervention Prioritization” and “Resource Allocation” sections below). In addition, published cost-effectiveness studies can be used to support advocacy efforts to obtain funding for particular interventions by demonstrating that the target intervention is an efficient use of HIV prevention resources.

This potential advocacy function is illustrated by Sweat and colleagues’ cost-effectiveness analysis of the VOICES/VOCES intervention. VOICES/VOCES is a single-session, video-based, interactive, group risk reduction intervention designed to be integrated into routine practice in STD clinics and similar settings that serve African American and Latino clients at high risk of HIV. Previous research demonstrated that the VOICES/VOCES was successful at reducing HIV-risk behaviors, especially among men with large numbers of sexual partners. The cost-effectiveness analysis indicated that this intervention was **cost-saving**, and especially so for male STD-clinic clients with large numbers of sex partners. The results of this analysis therefore could be used to advocate for increased funding of brief interventions such as VOICES/VOCES.

The cost-effectiveness of brief HIV prevention interventions also is illustrated by Pinkerton and colleagues’ (2002) analysis of the NIMH “Project Light” interventions. The authors conducted an *incremental* cost-utility analysis of the two interventions included in this scientific trial of intervention strategies. The control intervention consisted of a single 1-hour HIV/AIDS educational session in which participants viewed a videotape and discussed HIV prevention with trained facilitators. This basic intervention was compared to a 7-session, small group intervention that emphasized motivation, skills, and self-efficacy related to HIV risk reduction. The incremental cost-utility analysis consisted of two steps. First, the video intervention was compared to a no-program option. This analysis indicated that the video intervention was **cost-saving**—that is, society could realize a net economic advantage by offering this brief intervention to all persons at similar risk to participants in the NIMH prevention trial. Not surprisingly, the 7-session small-group intervention was substantially more expensive than the single-session intervention ($476 versus $56), but it also was much more effective at reducing participants' HIV risk, and therefore averted more infections. ***But did the greater impact justify the additional cost?*** In the second step of the analysis, Pinkerton and colleagues compared the small group intervention to the video intervention in order to determine the *incremental* cost-utility ratio of the former, relative to the later—that is, how much *more* did it cost per *additional* QALY saved? QALY refers to Quality-adjusted life years, a frequently used outcome measure to describe a year of healthy life. (See Section II for a detailed description.) For the men in the sample, the small group intervention was **cost-saving** in comparison to the video intervention, suggesting that the additional expenditure required by the more intensive intervention would be recouped by future savings in averted HIV-related medical care costs. The incremental cost-utility ratio for women participants was $33,000 per QALY saved, which is less than the $60,000 per QALY threshold commonly used to identify cost-effective interventions. The $60,000 threshold refers to the estimated point at which prevention costs are the about the same as the costs for HIV/AIDS care and treatment. Thus, for men, the video intervention would save money, and the small group intervention would save even more. For women, the video intervention was **cost-saving** and the small group intervention was a cost-effective (but not cost-saving) alternative.

Intervention Comparisons

Although several reviews of HIV prevention cost-effectiveness recently have appeared in the literature, great care is needed in comparing the cost-effectiveness of different interventions. The cost-effectiveness of a particular intervention, *for a particular population,* critically depends on the risk level of the population (see discussion in the section on "Targeting Prevention Efforts"). At the extreme, intervening with persons at zero baseline risk is likely to prove extremely cost-*ineffective*. Comparing the cost-effectiveness of interventions for different populations is like comparing apples and oranges. It is for this reason that the guidance on HIV prevention community planning recommends prioritizing interventions within specific populations, rather than across populations.

Methodological differences and differences in specific assumptions (e.g., about the correct values of epidemiological parameters) further complicate efforts at cross-study comparison. These differences are largely unavoidable due to the widely-varying nature of the interventions that have been evaluated. In order to compare cost-effectiveness results, one must look past these differences and assume that the analysts applied the most appropriate methods and parameter values in assessing the cost-effectiveness of the target interventions.

Pinkerton and colleagues (2001) reviewed the results of the economic evaluation literature related to HIV sexual risk reduction. The results of this review were arrayed in a series of population-specific "league tables" that listed the average **cost-effectiveness ratios** (gross program cost per infection averted) of interventions for each target population, together with program cost information and assumptions about the prevalence of infection utilized in the studies. The review included individual tables for men who have sex with men, at-risk men (a group that might or might not include some men who have sex with men), at-risk women, and counseling and testing programs.

Overall, approximately half the interventions included in this review were found to be **cost-saving**, and approximately three-fourths were cost-effective in comparison to other (non-HIV) health-related interventions and procedures. An intervention that can prevent an infection for less than the lifetime cost of treating a case of HIV/AIDS is said to be **cost-saving**, because the net economic impact of funding such an intervention is to save money in the long-run. (See Section II for a detailed description.) However, the authors cautioned readers against overinterpreting the results of this synthetic analysis, noting that interventions for a particular population might very well be complementary rather than mutually exclusive. For example, a person might benefit from participating in both a small-group intervention *and* by receiving free condoms as part of a condom distribution program. A note to consider, though, are that current evaluation techniques are not yet able to distinguish *how much* of each intervention is enough. One of the key assumptions is that all the circumstances around each intervention are roughly "equal." Thus, although ranking interventions by their **cost-effectiveness ratios** may help decision makers identify the most cost-effective interventions, the complementary nature of interventions must be taken into consideration.

Intervention Prioritization

How can cost-effectiveness information best be integrated into the intervention prioritization process? This is a complex question with no easy answers. **Cost-effectiveness** is only one of a number of important criteria that community planning groups and other decision makers need to consider when assessing the overall worth of different intervention strategies.

Several methods for completing the difficult task of setting priorities among HIV prevention interventions have been proposed in the literature. One of the simplest methods is the ranking method, in which a number of criteria (e.g., intervention cost-effectiveness, capacity of community-based organizations to implement specific interventions, sustainability, acceptability to the target community, etc.) are identified, then all possible interventions are ranked, one criterion at a time, according to how well they satisfy the criterion (see Johnson-Masotti, Pinkerton, Holtgrave, Valdiserri, & Willingham, 2000). For example, the intervention that is believed to be the most cost-effective would receive a ranking of "1" on this dimension, whereas the one that is thought to be the most sustainable would receive a "1" on the sustainability dimension. Each intervention's rankings on the different criteria are then added together to arrive at an overall score for that intervention. The intervention with the smallest overall score is given the highest priority.

A somewhat similar approach was suggested by Holtgrave (1994). In his relatively simple prioritization scheme, candidate interventions must first pass a three-pronged test to determine if they are legal, acceptable to the target population, and accessible to that population. Only interventions that satisfy all three criteria are considered further. Interventions are then awarded between 0 and 3 points on the basis of the available evidence regarding their effectiveness, cost-effectiveness, and grounding in behavioral science theory (a perfect score of 3 is accorded only those interventions that have a solid basis in behavioral science, and for which there is evidence of both effectiveness and cost-effectiveness). Those interventions with the highest score receive the highest priority[1].

Johnson-Masotti and colleagues (2000) proposed a novel prioritization technique based on multi-attribute utility theory. This technique is similar to both the ranking method and Holtgrave's proposal. It begins by identifying criteria on which the individual interventions will be rated, and by assigning "importance weights" to these criteria. The importance weights reflect the relative importance that the criteria will be accorded in the final, overall score. For example, using a 1 to 10 scale where 1 is the most important, cost-effectiveness might be assigned an importance weight of 5, legality a 10, and community acceptability a 7. Next, each intervention is assigned a score on each of criterion, for example, on a scale of 1 to 100. The final score for each intervention is the sum of the scores it received on the individual criteria, weighted by the importance weights associated with the criteria. The formula for calculating the overall score is fairly simple: Overall Score = (score on criterion #1)*(weight of criterion #1) + (score on criterion #2)*(weight of criterion #2) + ... The main advantage of this method is its flexibility. Different decision makers can identify different criteria and/or assign different importance weights to the criteria. The main drawback is its complexity.

Resource Allocation

The ultimate goal of estimating the economic efficiency ("**cost-effectiveness**") of interventions is to assist public health decision makers in the arduous task of determining how much money to invest in which interventions in a given time period and within a given budget. This implies some "priorities" may receive "zero" amounts. The amount of funds allocated towards an intervention will often dictate the number to be served. However, HIV prevention **resource allocation** presents a number of difficulties, and the literature on this important topic is relatively limited.

Resource allocation can be approached as an optimization problem: the question is how HIV prevention funds should be allocated so as to maximize some objective criteria, such as the number of infections averted. For example, we can envision a simple (and very unrealistic) scenario in which there are several candidate interventions, each serving a different population. To maximize the number of infections averted, the intervention with the smallest **cost-effectiveness ratio** (cost per infection averted) should be funded first, followed by the intervention with the next smallest cost-effectiveness ratio, and so on, until the HIV prevention budget is exhausted. Note, however, this method does not indicate how much funding should be budgeted for each intervention. One would need additional information about how many people could feasibly be reached by each successive candidate interventions and at what cost per person. This information is not provided in the cost-effectiveness ratio.

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[1] Note: The scoring system by Holtgrave (where the interventions with the highest score receive highest priority) is organized differently from that of Johnson-Masotti (where the intervention with the smallest score receives the highest priority. For purposes of this review, the work of the original authors was not modified.

The situation is more complicated if there are multiple competing (or complementory) interventions for the same population. To select a *single* intervention from among a range of alternatives for a particular population, the following steps are required. First, all the interventions are ranked according to effectiveness. Secondly, any intervention that costs more but is less effective than one or more alternative interventions is eliminated from the list. In the next step, an **incremental cost-effectiveness ratio** is computed for each pair of adjacent interventions listed in the effectiveness ranking. These incremental ratios tell us how much more each successively more effective intervention costs, per additional infection averted, than the next most effective alternative. Resources are then allocated to interventions based on the incremental cost-effectiveness ratios and the available budget. Karlsson and Johannesson (1996) describe this technique in detail. The main drawback to this approach is that it ignores the possibly complementary or synergistic nature of interventions for the same population. Often, more than one intervention for a particular population will be needed or desired.

Kaplan (1998) described a somewhat more general resource allocation technique based on optimization theory. In this model, each candidate intervention is associated with a function that specifies, for any given funding level, how many infections would be averted if the intervention were funded at this level. These "production functions" can be expressed symbolically as $A_k(c_k)$, where A_k denotes the number of infections that would be averted by intervention number *k* when funded with c_k dollars. To make things a bit more concrete, we'll assume here that there are 3 candidate interventions. If we spend c_1 dollars on intervention #1, c_2 dollars on intervention #2, and c_3 dollars on intervention #3, then the total cost is $c_1 + c_2 + c_3$ dollars. The production functions associated with the 3 interventions tell us that allocating resources in this way would prevent a total of $A_1(c_1) + A_2(c_2) + A_3(c_3)$ infections.

The goal of Kaplan's method is to prevent as many infections as possible—that is, to maximize $A_1(c_1) + A_2(c_2) + A_3(c_3)$—by choosing c_1, c_2, and c_3 wisely. Obviously, overall spending cannot exceed the available HIV prevention budget B, so we must make sure that $c_1 + c_2 + c_3 \leq B$. Remember, c_1, c_2, and c_3 are not fixed; they are the unknown quantities that we are trying to determine (i.e., they are the answers to the question of "how much" to spend on each intervention). In particular, we want to find values of c_1, c_2, and c_3 such that: (1) $c_1 + c_2 + c_3 \leq B$; and (2) $A_1(c_1) + A_2(c_2) + A_3(c_3)$ is maximal. In the example shown in the table below, Scheme #3 is the best resource allocation scheme because it results in the greatest number of averted infections for the same $500,000 available. In practice we would want to consider *all possible ways* to allocate the budget across the candidate interventions, not just a few specific allocation schemes. Mathematical techniques can be used to consider all possible schemes simultaneously to arrive at the optimal resource allocation scheme that maximizes the number of infections averted without exceeding the available HIV prevention budget.

The main drawback of Kaplan's resource allocation method is immediately obvious: to implement this method requires that we know how many infections could be averted by each candidate intervention at every possible funding level. This difficulty is not easily overcome. The cost-effectiveness ratio-based resource allocation method outlined above requires less detailed information, but still requires that we know the **cost-effectiveness ratios** for all candidate interventions. These information requirements are unavoidable if resource allocation decisions are to take into account both costs and expected impact.

A second limitation of both of the methods reviewed above is that they focus on a single objective, preventing infections, and ignore social, political, and other important considerations faced by HIV prevention resource allocation decision makers. In particular, these methods do not take into account the prioritization recommendations of local community planning groups.

Table: Three possible ways to allocate a $500,000 HIV prevention budget across three candidate interventions (X, Y, Z)

	Resources allocated to intervention	**Infections averted at this funding level**
Allocation Scheme #1 (A_1)	**Cost (C) in dollars**	
Intervention X	$200,000	5
Intervention Y	$200,000	2
Intervention Z	$100,000	3
Total for all interventions	**$500,000**	**10**
Allocation Scheme #2 (A_2)	**Cost (C) in dollars**	
Intervention X	$200,000	5
Intervention Y	$100,000	1
Intervention Z	$200,000	5
Total for all interventions	**$500,000**	**11**
Allocation Scheme #3 (A_3)	**Cost (C) in dollars**	
Intervention X	$100,000	4
Intervention Y	$100,000	1
Intervention Z	$300,000	7
Total for all interventions	**$500,000**	**12**

Allocation Scheme #3 (A_3) provides for averting the greatest number of infections relative to Scheme #1 (A_1) or Scheme #2 (A_2). Note that this is accomplished by budgeting less for Intervention X and Y and putting more funding into Intervention Z. This change in allocation suggests that less of Intervention X and Y will be done (indicating that fewer people will be served with those interventions) and more effort will be put into Intervention Z (where more people would be served).

Section III. Relevant Concepts

Organization

This summary of relevant concepts and terminology is organized in outline format (see below for an alphabetical listing of terms). Each section of the outline begins with a brief overview of the topic covered by the section. Individual terms are then defined. Several useful references are listed at the end of this section.

A0. Community Planning
- A1. Priority Setting
- A2. Resource Allocation

B0. Economic Evaluation
- B1. Cost Analysis
    - B1a. Economic (Opportunity) Costs and Finanacial Costs
    - B1b. Fixed and Variable Costs
    - B1c. Common Year Dollars
    - B1d. Discounting
- B2. Cost-benefit Analysis
- B3. Cost-effectiveness Analysis
    - B3a. Average Cost-effectiveness Ratios
    - B3b. Incremental Cost-effectiveness Ratios
    - B3c. Marginal Cost-effectiveness Ratios
    - B3d. Which Ratio?
- B4. Cost-utility Analysis
- B5. Threshold Analysis
- B6. Cost-saving Interventions
    - B6a. Gross Cost and Net Cost
- B7. “Cost-effective” as an Adjective

C0. Economic Evaluation and Study Design
- C1. Prospective and Retrospective Analysis
- C2. Time Horizon
- C3. Perspective
- C4. Base-case and Sensitivity Analysis

D0. Modeling Intervention Effectiveness
- D1. Risk of Infection
- D2. Primary and Secondary Infections
- D3. Mathematical Models
  - D3a. Bernoulli Models
  - D3b. Proportionality Models
  - D3c. Population Models

E0. Limitations of Economic Evaluation Literature

Alphabetical Listing of Topics

The citation (usually a letter followed by a number, e.g., "A2") listed in parentheses after each term below refers to the relevant section of the outline (e.g., "A") and the subsection ("2") in which the term is discussed. For example, "Average cost-effectiveness ratio (B3a)" indicates that average cost-effectiveness ratios are discussed in Definition 3a of Section B.

- Average cost-effectiveness ratio (B3a)
- Base-case analysis (C4)
- Bernoulli model (D3a)
- Common year dollars (B1c)
- Community planning (A0)
- Comparability (E0)
- Cost analysis (B1)
- Cost-beneficial (B2)
- Cost-benefit analysis (B2)
- Cost-effective (B7)
- Cost-effectiveness analysis (B3)
- Cost-effectiveness ratio (B3)
- Cost-saving (B6)
- Cost-utility analysis (B4)
- Cost-utility ratio (B4)
- Discounting (B1d)
- Economic evaluation (B0)
- Fixed costs (B1b)
- Generalizability (E0)
- Gross cost (B6a)

- Incremental cost-effectiveness ratio (B3b)
- Limitations (E0)
- Marginal cost-effectiveness ratio (B3c)
- Mathematical models (D3)
- Net cost (B6a)
- Opportunity costs (B1a)
- Perspective (B3)
- Population models (D3c)
- Present value (B1d)
- Primary infections (D2)
- Priority setting (A1)
- Proportionality models (DC3b)
- Prospective analysis (C1)
- Quality-adjusted life year (QALY) (B4)
- Resource allocation (A2)
- Retrospective analysis (C1)
- Risk of infection (D1)
- Secondary infections (D2)
- Selection bias (E0)
- Sensitivity analyses (C4)
- Societal perspective (C3)
- Threshold analysis (B5)
- Time horizon (C2)
- Variable costs (B1b)

Discussion of Topics

A0. Community Planning

HIV prevention community planning is a collaborative process through which health departments work in partnership with community planning groups (CPGs) to design local prevention plans that best represent the needs of the various communities at risk for, or infected with, HIV.[2] CPGs consist of members from health departments, community-based organizations (CBOs), local communities, and others. In December 1993, the Centers for Disease Control and Prevention (CDC) initiated HIV prevention community planning by issuing the *Supplemental Guidance on HIV Prevention Community Planning for Noncompeting Continuation of*

[2] Academy for Educational Development, Center for Community-based Health Strategies. (1999). HIV Prevention Community Planning: An Orientation Guide. Washington DC: AED.

Cooperative Agreements for HIV Prevention Projects, also known as the *Guidance*.[3] This *Guidance* is the blueprint for HIV prevention community planning and provides flexible direction to grantees (65 state, local, and territorial health departments, or project areas) receiving federal HIV prevention funds to design and implement a participatory community planning process. (Please note that CDC was engaged in a process to develop an updated *Guidance* as of the writing of this guide to the literature.)

The role of HIV prevention community planning groups is to set priorities among: (1) populations at risk for HIV infection, and (2) HIV prevention interventions to meet the needs of priority populations. The planning group's recommended priorities form the basis for the health department's application to CDC for HIV prevention funds, in which the health department outlines its plan for allocating (i.e., distributing) HIV prevention resources within its jurisdiction. These priorities can be used to inform other funders as well.

The *Guidance* specifically states that "available information on the relative costs and effectiveness of proposed strategies and interventions (either demonstrated or probable)" should be considered in prioritizing populations and interventions. Other statements where cost-effectiveness is mentioned in the *Guidance* are shown in the box below. In short, cost-effectiveness considerations are expected to play a role in CPG's **priority setting** process.

It is important to understand that community planning groups do not control, nor make decisions regarding, the resources needed to fund the priorities they have identified. It is the health department's responsibility to allocate HIV prevention resources, guided by the CPG's priority recommendations. Cost-effectiveness information can play a role in this process as well, as described in the section on "Resource Allocation."

Box: References to cost-effectiveness in the *Supplemental Guidance on HIV Prevention Community Planning*

HIV Prevention Community Planning Core Objectives

Core Objective #4—Ensuring that interventions are prioritized based on explicit consideration of priority needs, outcome effectiveness, cost and ***cost-effectiveness****, theory, and community norms and values.*

Roles and Responsibilities

The role of the planning group(s) in the HIV prevention community planning process is to…carefully review available epidemiologic, evaluation, behavioral and social science, cost and ***cost-effectiveness****, needs assessment, and resource inventory data and other information required to identify and prioritize HIV prevention needs.*

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[3] Centers for Disease Control and Prevention. *Guidance: HIV Prevention Community Planning for HIV Prevention Cooperative Agreement Recipients.* Atlanta, GA: CDC, 1998.

*Centers for Disease Control and Prevention shall…provide technical/program assistance through a variety of mechanisms to help recipients understand how to…identify and evaluate effective and **cost-effective** HIV prevention activities for these priority populations.*

Source: Centers for Disease Control and Prevention. *Guidance: HIV Prevention Community Planning for HIV Prevention Cooperative Agreement Recipients.* Atlanta, GA: CDC, 1998.

A1. Priority Setting

HIV prevention community planning groups are required to identify high-priority populations at risk for HIV infection, and to prioritize interventions targeted to these populations. Target population priorities are based on consideration of epidemiological profiles, needs assessments, resource inventories, and gap analyses. CDC asks that HIV prevention planning groups base their recommendations for interventions for each of the priority populations on factors such as evidence that the intervention targets a specific population, that it has proven effective in changing risky behavior, and that it is acceptable to the target audience. CDC also asks planners to consider the cost-effectiveness of interventions. The community planning group describes its recommendations in a comprehensive prevention plan. This comprehensive prevention plan is the basis for the Health Department's request for funding from CDC. This plan should also provide guidance to any other funders seeking to support prevention in a particular jurisdiction.

A2. Resource Allocation

Based on the CPG's recommendations, the health department drafts its prevention funding application for submission to CDC. The health department is then responsible for allocating the HIV prevention resources it receives from CDC. Resource allocation refers to the distribution of HIV prevention funds to support interventions in at-risk populations. Resource allocation is the process of "dividing up the pie." This process should be informed by the population and intervention priorities set by local HIV prevention community planning groups.

B0. Economic Evaluation

Economic evaluation techniques are used to measure the cost and/or the "economic efficiency" of HIV prevention interventions and other services. Economic efficiency refers to getting the greatest outcome at the least cost, or "the best bang for the buck." Cost analysis forms the basis for all economic evaluation strategies. However, knowing the cost of an intervention is not enough. It is important also to take into account the benefits of the intervention. Economic evaluations techniques such as **cost-benefit analysis**, **cost-effectiveness analysis**, and **cost-utility analysis** can be used to quantify the trade-off between costs and benefits. An “economically-efficient” (or “cost-effective”) intervention is one that produces a good balance of benefits to costs, in comparison with other interventions or other social programs.

B1. Cost Analysis

Cost analysis is the process of estimating the cost of a prevention activity, such as an HIV prevention intervention. The main outcome measure of a cost analysis is an estimate of the cost of running the intervention. (The cost estimate can later be combined with an estimate of the effectiveness the intervention to determine its overall cost-effectiveness.) Sometimes the total cost of the intervention is reported; other times costs are presented on a per-client basis. The main costs for most HIV prevention interventions are staff costs (salary or hourly compensation, plus fringe benefits); facility costs (rental, utilities, insurance, etc.); materials (condoms, sterile syringes, printed material, etc.); transportation expenses; and—particularly in research settings—incentives paid to participants.

B1a. Economic (Opportunity) Costs and Financial Costs

There are two kinds of the costs: economic costs and financial costs. The financial costs of an intervention are the actual monetary outlays necessary to produce the intervention. These are the costs that appear in the intervention budget and in the records of actual intervention expenses. In contrast, the economic costs of the intervention are the ***opportunity costs*** associated with all resources used in implementing the intervention, whether paid for or not. For example, the opportunity cost associated with donated meeting space (to conduct a small-group intervention, for instance) is the cost borne by the donor who has foregone the opportunity to rent the meeting space to a paying customer. Intervention participants also incur opportunity costs associated with the time that they spend participating in the intervention; this is time that they could have spent earning money at work, or spent as leisure time, which also is valuable. Thus, opportunity costs are more inclusive than financial costs—the opportunity cost of an intervention includes the cost of all resources consumed in the intervention, whether a monetary expenditure was required (financial cost) or not. As discussed below in the “**Perspective**” section, most economic evaluation studies (i.e., **cost-benefit**, **cost-effectiveness**, and **cost-utility analyses**) report the economic cost of the intervention, which is greater than the financial cost.

B1b. Fixed and Variable Costs

Intervention costs can be classified as either fixed costs or variable costs. Variable costs change proportionately with a change in volume of the activity, such as the number of clients. For example, the cost of condoms distributed as part of an intervention would change depending on number of persons served during a particular time period. Fixed costs, on the other hand, do not vary with the volume of the activity, up to a limit. Rent, utilities, and some administrative costs are all examples of fixed costs. For instance, the rental cost for a particular meeting space that holds 50 people will be the same fixed cost whether 50 people attend or any number less. However, if 51 people attend, additional meeting space will be required at an additional fixed cost.

B1c. Common Year Dollars

Typically, all costs are expressed relative to a common year in order to eliminate any discrepancies due to inflationary effects. For example, all costs might be converted to year 1999 dollars using the Consumer Price Index. Likewise, before comparing the cost of one intervention to the cost of another evaluated in a different year, all intervention costs should be converted to common year dollars (i.e., express the costs of both interventions in the same common year). An intervention that cost $10,000 in 1995 year dollars actually might be more expensive than one that cost $11,000 in 2002 year dollars.

B1d. Discounting

As a general rule, most people prefer to receive benefits in the present and to delay costs into the future. Because of this, money that we receive in the future, or that we spend in the future, is worth less than money that we receive or spend in the present. This is the basis for our credit-driven economy: in order to gain benefits in the present, people are willing to pay more in the future. Economists and accountants use a technique known as **discounting** to convert future costs and benefits into their ***present values***. For example, the present value of $100 received one year in the future is $97, using an annual discount rate of 3%. (The discount rate reflects the strength of society's preference for gaining benefits now, but paying costs later; a 3% rate is fairly standard.) In other words, most of society would be willing to accept $97 today, rather than waiting one year to receive $100. Economic analyses take this preference into account by discounting all future costs and all future benefits into their **present value** equivalents.

B2. Cost-benefit Analysis

Cost-benefit analysis is one of the oldest economic evaluation techniques, but it seldom is used to evaluate HIV prevention interventions. The main question addressed by a cost-benefit analysis is whether the program is *cost-beneficial*—that is, whether the benefits of the program outweigh the costs. Answering this question requires assigning a monetary value to all benefits, so that the benefits can be directly compared to the costs. The benefits of preventing HIV infection include longer life, better health, improved quality of life, savings in HIV/AIDS-related medical care costs, and averted productivity losses (as well as benefits to friends, relatives, and society as a whole). It is very difficult to assign a monetary value to these important and quite varied benefits.

Cost-benefit analysis typically is used to determine whether or not there is a net savings from a particular program or project (such as building a bridge). Cost-benefit analysis is not particularly useful for comparing one program to another, and for this reason—together with the difficulty of assigning monetary values to the many benefits of HIV prevention—it has limited applicability to HIV prevention.

B3. Cost-effectiveness Analysis

The main outcome in a cost-effectiveness analysis is a ratio of costs to the specific benefits, expressed in natural, health-related units, such as life-years saved or HIV infections averted. This way of expressing benefits facilitates comparisons between different HIV prevention interventions, all of which can be expressed in a common metric, such as cost per HIV infection averted.

B3a. *Average Cost-effectiveness Ratios*

Most of the cost-effectiveness ratios reported in the literature are average ratios. These ratios tell us how much money the given intervention costs per HIV infection averted (or per life year saved, etc.) compared to a "no-intervention" option. The average cost-effectiveness ratio can be written: CER = C/E, where C and E are the cost and effectiveness of the intervention. This implies that the lower the cost and the greater the effectiveness, the smaller the ratio. That is, one gets more (greater) effect for less expenditure, which is a good thing. (From this expression it should be clear than an intervention with zero effectiveness would have an undefined cost-effectiveness ratio. Therefore, evidence of effectiveness is required before a cost-effectiveness analysis can be conducted.) For instance, suppose there would be 4 new infections in the population without the intervention, but only 2 new infections with the intervention. The intervention therefore prevents 2 new infections. If it costs $600,000 to implement, then the average cost-effectiveness ratio is $600,000/2 = $300,000 per infection averted.

B3b. *Incremental Cost-effectiveness Ratios*

Suppose we are thinking of replacing the intervention described above with a new, more expensive intervention *for the same population*. The question now is not whether the new intervention is cost-effective compared to doing nothing. Instead, we need to know whether the new intervention is cost-effective compared to the existing intervention. Thus, we need to know the incremental cost-effectiveness of the new intervention, relative to the existing one. The incremental cost-effectiveness ratio can be written: CER = $(C_1 – C_2)/(E_1 – E_2)$, where C_1 and E_1 are the cost and effects (e.g., infections averted) of Intervention #1, and C_2 and E_2 are the cost and effects of Intervention #2. For example, suppose the new intervention prevents 3 infections at a total cost of $1 million. Compared to the existing intervention, which prevented 2 infections for $600,000, the new intervention has an incremental cost-effectiveness ratio of ($1,000,000 – $600,000)/(3 – 2) = $400,000 to avert the additional infection. The two options are thus: (1) stick with the existing intervention, which costs $300,000 per infection averted, or (2) replace it with the new intervention, which costs $400,000 for the *additional* infection averted.

B3c. *Marginal Cost-effectiveness Ratios*

A marginal cost-effectiveness ratio sometimes is used to assess the extra costs and extra benefits achieved by expanding an existing program. Marginal ratios are closely related to **incremental ratios** (both compare one "program" to another), and the terms are sometimes used interchangeably. We can think of the marginal ratio as reflecting the incremental cost-effectiveness ratio produced by comparing two interventions: the current intervention, and a second, *identical* intervention that provides services to one more person than the first. For example, suppose we are thinking of expanding an HIV prevention intervention to reach more people, and that, for each additional person served, the cost of the program increases by $500 and the number of infections averted increases by one-one-thousandths (i.e., the program would need to reach 1000 more people to prevent one additional infection). The marginal cost-effectiveness ratio is the additional cost per additional health-outcome: \$500/0.001 = \$500,000 per additional infection averted.

B3d. Which Ratio?

The average cost-effectiveness ratio tells us how much an intervention costs per HIV infection averted. Average cost-effectiveness ratios are useful for comparing different interventions for the same population. For example, an intervention that costs \$300,000 per infection averted is more cost-effective than one that costs \$400,000 per infection averted. This would be used to rank order like interventions for the same population to help choose which <u>one</u> to implement.

The average cost-effectiveness ratio implicitly compares the intervention to a "do nothing" program that costs nothing and prevents no infections. But what if there already is a prevention program in place, and we are considering replacing it with a different intervention that is both more effective and more costly? In this situation, we might compute the **incremental cost-effectiveness ratio**, which tells us how much *more* the second program costs to achieve the greater outcome. (Sometimes, one intervention is both more effective and less costly than an alternative. In this case there is no need to compute an incremental cost-effectiveness ratio—the more effective, less expensive intervention is clearly superior to the alternative.)

Finally, if we are considering expanding an existing program (by serving more clients, for example), then we might be interested in the **marginal cost-effectiveness ratio**, which tells us how much more the expanded program costs per each additional infection averted.

B4. Cost-utility Analysis

A cost-utility analysis is a special type of cost-effectiveness analysis in which benefits are expressed as the number of **quality-adjusted life years** (**QALYs**) saved by an intervention. The basic idea behind quality-adjusted life years is that each year of life that is spent in a particular health state can be assigned a weight between 0 and 1 that indicates the health-related quality of life enjoyed by someone in that health state. A weight of 1 indicates perfect health, whereas 0 denotes the complete absence of health (i.e., death). In theory, QALY weights should reflect society's preference for different health states. At the extremes, of course, people would rather be alive than dead, but they would also rather spend a year with a broken arm than spend a year on dialysis. Therefore, the QALY weight associated with having a broken arm is greater than the weight for dialysis.

The use of QALYs permits us to compare across health care and health promotion for different health concerns. It also permits us to take into account morbidity as well as mortality. Some health-related procedures and interventions are meant only to extend life, others are meant only to improve the quality of life, and some do both. Cost-utility analysis allows us to compare these different sorts of interventions using a common metric: cost per QALY saved.

HIV infection can have profound consequences for both morbidity and mortality. For example—using made-up QALY weights and other parameter values *just for the sake of illustration*—suppose that an average 30-year person lives to age 70 in very good health, with a QALY weight of 0.95 for every year up to age 60, and a QALY weight of 0.9 for each year thereafter. The total number of QALYs for this person is: 30*0.95 + 10*0.9 = 37.5. Now suppose that this person became infected with HIV at age 40, and lived 20 years with HIV, with a QALY weight of 0.85, before dying at age 60. His or her QALY total is: 10*0.95 + 20*0.85 = 26.5. Therefore, he or she has "lost" 11 QALYs (37.5 – 26.5) due to HIV. An intervention that had prevented him or her from becoming infected from age 30 on would therefore have "saved" 11 QALYs.

The main outcome of a **cost-utility analysis** can be expressed as an average cost-utility ratio (cost per QALY saved by a program), an incremental cost-utility ratio (additional cost per additional QALY saved by one program, relative to another), or a marginal cost-utility ratio (additional cost per additional QALY saved by expanding a program).

Although **cost-utility analysis** is widely used in evaluating the cost-effectiveness of HIV prevention interventions, the cost-effectiveness ratio (cost per infection averted) is more useful than the **cost-utility ratio** (cost per QALY saved) for comparing different HIV prevention interventions. Fortunately, most published cost-utility analyses also include an estimate of the cost-effectiveness ratio.

B5. Threshold Analysis

Sometimes the cost of an intervention is known, but the number of HIV infections averted cannot be estimated, or perhaps effectiveness can be estimated but the cost is unknown. Threshold analysis allows us to draw tentative conclusions about the expected cost-effectiveness of the intervention, despite the missing data, by making use of a threshold value. For example, suppose we know that an intervention cost $2 million, but we do not know how many infections it averted. Suppose also that there is general agreement that interventions that cost less than $1 million per infection averted can be considered cost-effective. The question is, how many infections would the intervention need to have averted to be considered cost-effective using the $1 million per infection averted criterion? Using simple arithmetic we can compute an "infections averted threshold." We find this "infections averted threshold" by dividing the amount spent on the intervention ($2 million) by the maximum of $1 million per infection averted threshold. The intervention would be cost-effective if it averted two or more infections ($2 million/$1 million). [The "units" (millions of dollars) cancel out and thus, your answer is that if *at least* two infections could have been averted, then this intervention would be considered **cost-effective**. The threshold value is $1 million per case averted. This is unlike the threshold value of $60,000 per QALY which was described on page 11.] If there is solid evidence that the intervention did indeed prevent at least 2 infections, then we can conclude that the intervention is cost-effective even though we do not know the exact number of infections averted. [See Section B7 for more about using "cost-effective" as an adjective.]

B6. Cost-saving Interventions

One of the main economic benefits of preventing HIV infection is the associated savings in HIV/AIDS-related medical care costs. Averting an infection also averts these future costs, which have been estimated at approximately $200,000 in discounted, year-2000 dollars. (Because of the ever-changing nature of HIV therapies and advances in the prevention and treatment of opportunistic infections and other consequences of HIV disease, estimates of the lifetime medical care cost associated with HIV infection are somewhat uncertain.)

An intervention that can prevent an infection for less than the lifetime cost of treating a case of HIV/AIDS is said to be *cost-saving*, because the net economic impact of funding such an intervention is to save money in the long-run. The term "cost-saving" is much more conservative than "**cost-beneficial**" (see section on Cost-benefit Analysis) because it balances the cost of the intervention only against the expected savings in medical care costs; it does not take into account the other benefits of preventing HIV infection. A cost-saving intervention is cost-beneficial, but the reverse is not necessarily true (a cost-beneficial intervention might not be cost-saving).

The average cost-effectiveness ratio for an HIV prevention intervention is just the cost per infection averted by the intervention. If this ratio is less than the cost of HIV/AIDS medical care, then the intervention is cost-saving. Similarly, the **incremental cost-effectiveness ratio** comparing one intervention to a more expensive and more effective alternative indicates the additional cost per additional infection averted by the second intervention, relative to the first. If this ratio is negative (indicating that the second intervention can prevent additional infections at an additional cost that is less than the cost of treating the additional infections), then the second intervention is said to be cost-saving relative to the first.

B6a. Gross Cost and Net Cost

The gross cost of an intervention is simply the total program cost. Some cost-effectiveness and cost-utility analyses report the net cost of an intervention, rather than the gross cost. The **net cost** is obtained by subtracting from the gross cost the future savings in averted HIV/AIDS-related medical care costs resulting from the prevention of infections. An intervention is **cost-saving** if either the gross cost per infection averted is less than the lifetime cost of treating HIV disease, or if the net cost is negative (these two formulations are entirely equivalent). For example, an intervention that costs $300,000 and prevents 2 infections has a gross cost per infection averted of $300,000/2 = $150,000, which is less than the $200,000 estimated lifetime cost of HIV/AIDS care, and a net cost of $300,000 – 2*$200,000, which is less than zero.

B7. "Cost-effective" as an Adjective

What does it mean to say that an intervention is "cost-effective"? Unfortunately, the use of "cost-effective" as an adjective can be confusing. Saying that an intervention is "cost-effective" is a shorthand way of saying that it is a better use of limited health-related resources than are other possible uses for these resources, such as funding organ transplants or fluoridating the water supply. Although there is no set cut-off for determining whether a particular health-related program is or is not cost-effective, most analysts agree that programs that can save a QALY for $50,000 to $60,000 can be considered cost-effective, whereas those with **cost-utility ratios** in excess of $200,000 per QALY saved are probably not cost-effective (notice that there is a large gray area between approximately $60,000 and $200,000 per QALY saved). Most of the HIV prevention interventions that have been evaluated to-date cost less than $50,000 to $60,000 per QALY saved and therefore are cost-effective in this sense. That is, HIV prevention is a good "buy" compared to other health-related programs which cost more than $60,000 per QALY. This $60,000 per QALY value was described in greater detail on page 11 of this guide.

For the purposes of choosing *among* different HIV prevention interventions, the more important question is: which intervention for a particular population group is the *most* cost-effective? That is, which one saves the most lives (or years of life) for the given spending level? This very difficult question is discussed further in the "Resource Allocation" literature overview.

C0. Economic Evaluation Study Design

The two main steps in conducting a cost-effectiveness or **cost-utility analysis** of an HIV prevention intervention are: first, assessing the cost of the intervention (described above in the "**Cost Analysis**" section), and second, estimating the number of infections averted by the intervention (see the "Modeling Intervention Effectiveness" section, below). In this section we present some general comments on overall study design.

C1. Prospective and Retrospective Analyses

Cost analyses can be conducted retrospectively or prospectively, or using a mixed strategy. A retrospective cost analysis is one that is conducted after the intervention has already been completed. Cost information is obtained from existing records, estimates of the current costs of materials, rent, and so forth, and from interviews with key intervention staff. In contrast, in a prospective cost analysis, cost data are collected while the intervention is on-going.

C2. Time Horizon

Intervention costs usually are measured for some fixed period of time. This time period might cover the entire life of a one-time intervention, or it might be some portion (e.g., one year) of an on-going intervention. Only the costs that are incurred within the **time horizon** are included in the **cost analysis**. In contrast, the effectiveness of an intervention might well extend beyond this period, for example, by inducing life-long adoption of risk reduction practices.

C3. *Perspective*

The perspective of an economic evaluation study (e.g., cost-effectiveness analysis) determines which costs and benefits will be included in the analysis. For example, an analysis conducted from the perspective of the community-based organization (CBO) implementing a particular intervention might include only those costs directly borne by the CBO. This might not represent the total cost of the intervention (e.g., the CBO might make use of facilities provided free by the state, which must absorb these costs).

The most comprehensive perspective is the societal perspective. The **societal perspective** includes all costs and all benefits (or other consequences) of the intervention, regardless of who pays for the costs or enjoys the benefits. In the example above, a **cost analysis** from the societal perspective would include all costs to the state as well as those borne by the CBO. It also would include any costs incurred by participants in the intervention. The societal perspective attempts to estimate the true *economic* costs associated with the intervention (see section on "Economic Costs and Financial Costs"). However, some published papers on the cost-effectiveness analysis of HIV prevention interventions do not include the full economic cost even if the authors claimed that the societal perspective was used in the studies. The most common case is that the costs to the clients for participating in the intervention, or to receive the service, was not included in most studies.

C4. *Base-case and Sensitivity Analyses*

Usually, there is considerable uncertainty in the data used in economic evaluation studies. This uncertainly arises from several sources. The exact value of epidemiological parameters may not be known; intervention participants may not be completely honest in self-reporting their risk behaviors; a completely accurate accounting of intervention costs may be impossible to achieve; or the sample of people who participated in the intervention may not be wholly representative of the target community. To address this uncertainty, most economic evaluation studies include multiple sensitivity analyses in addition to a base-case analysis. The base-case analysis is based on the most plausible parameter values and therefore represents the analysts' best guess at the true cost-effectiveness of the intervention.

In the sensitivity analyses, the key parameters are varied—one or more at a time—within a range of plausible values and the cost-effectiveness ratio (or other outcome measure) is recalculated. This allows the analyst and readers to assess how stable the results are, and how much confidence should be placed in them. If the results do not change very much when key parameters are varied, then the results can be accepted without too much trepidation. On the other hand, if changing one or more of the parameters to a different but still plausible value causes a substantial change in the cost-effectiveness ratio, then the results of the base-case analysis should be accepted with caution, if at all.

D0. Modeling Intervention Effectiveness

Fortunately, the incidence of HIV in most communities in the U.S. is small compared to many parts of the world. Consequently, because most interventions serve a relatively small number of clients, only a very small number of new infections would be expected among the clients in any given time period. It therefore is difficult to evaluate the true number of infections averted by an intervention by looking at changes in incidence before and after the intervention. Instead, most cost-effectiveness analyses rely on **mathematical models** to translate behavioral changes into changes in the expected incidence of HIV infection, or equivalently, into an estimate of the number of infections averted by the intervention.

D1. Risk of Infection

In the literature the term "risk" often is used as a synonym for the wordier phrase, "probability of infection." By helping clients change the behaviors that place them at risk of infection, or by changing the environment in which risk-taking behaviors occur, HIV prevention interventions can reduce the probability that clients will become infected. To illustrate this point, imagine a population of 100 identical people whose risk-taking behavior results in a three-in-ten (i.e., 0.3) probability of becoming infected with HIV in the next year. This means that, on average, we would expect there to be 0.3*100 = 30 new infections within this group in the next year. We cannot say which 30, we can only give a group average. Now suppose that an intervention is conducted which reduces each person's risk (probability of infection) to one-in-ten (i.e., 0.1). Thanks to the intervention, we would expect there to be only 0.1*100 = 10 new infections in this group. The intervention therefore has averted 20 new infections. Again, we cannot say which intervention clients were spared infection, only that, as a group, 20 people who would have become infected didn't, as a result of the intervention.

D2. Primary and Secondary Infections

Some intervention participants are uninfected when they begin the intervention, and some are already infected. The goal of the intervention in the former situation is to help uninfected people stay that way, whereas in the latter situation, the intervention can help reduce the likelihood of HIV spreading further. The term "averted primary infections" is sometimes used in the literature to denote infections prevented among uninfected intervention participants. In contrast, "averted secondary infections" are infections that are prevented among the partners of already-infected intervention participants. Most cost-effectiveness analyses estimate the number of averted primary infections, and some also estimate the number of averted secondary infections. In either case, the estimated number of infections averted underestimates the true impact of the intervention because it does not take into account infections that are prevented among partners of partners, and their partners, and so on. Some analyses attempt to take into account these "downstream" infections by using **mathematical models** that look at the impact of the intervention on the population as a whole.

D3. Mathematical Models

Several different types of mathematical models are used in the literature to estimate the number of infections averted by HIV prevention interventions. Only a very brief overview is provided here.

D3a. Bernoulli Models

The basic Bernoulli Model is conceptually simple. In this model HIV transmission is treated as a probabilistic event. There are two components that affect the probability of transmission. The first is the probability that one partner is already infected and the other is not. Clearly, if neither is infected, or both are, then a new infection cannot result.

The second component is the probability that HIV is transmitted given that one partner is already infected. Each potentially risky episode (e.g., act of intercourse or injection with a previously-used syringe) is treated as a probabilistic event: either HIV is transmitted or it isn't. Imagine rolling a many-sided die. The die might have 10, 100, or many thousands of sides, but only one is marked "HIV transmission." The number of sides (i.e., the probability of transmission) is determined by multiple factors, such as—for sex––the particular sex act (e.g., receptive vs. insertive intercourse) and whether or not a condom was used. (The per-act probability of transmission associated with a particular sex act is sometimes called the *infectivity* of that sex act.) Obviously, the more times a risky behavior is repeated, the greater the likelihood that HIV will be transmitted. Similarly, if you roll a pair of dice enough times, snake-eyes *usually* will come up eventually.

The Bernoulli model takes information about the risk behaviors of individuals (e.g., number of sex partners, number and types of sex acts with these partners, condom use; or number of syringe-sharing partners, number of injections with shared syringes, use of bleach) and combines this information with epidemiological data (prevalence of infection in the community, probability of transmission associated with the particular act, effectiveness of condoms or bleach) to arrive at an overall estimate of the individual's probability of becoming infected. These infection probability estimates are then combined into an overall estimate of the number of infections expected among the cohort of individuals, given the behavioral risks they reported. By comparing the number of infections that would be expected with an intervention to the number expected without the intervention, the number of infections averted by the intervention can be estimated.

D3b. Proportionality Models

Another simple type of model assumes that intervention-induced changes in risk behavior are mirrored by opposite changes in HIV incidence. For example, if an intervention results in a 50% increase in condom use, then a 50% decrease in incidence would be expected. Provided that an estimate is available of the baseline incidence of infection (i.e., the incidence in the absence of intervention), the number of infections averted can be calculated. For instance, suppose the baseline incidence among a group of 5000 intervention participants is one-in-one-hundred (0.01). If each participants increases his or her condom use by 50%, then—according to this model—we would expect a 50% drop in incidence (to 0.005). Thus, the expected number of new infections is decreased from 5000*0.01 = 50 to 5000*0.005 = 25. Comments: This model should not be applied to target populations with two or more risk behaviors, such as MSM/IDU, unless an intervention results in the same rate of behavior change, e.g. the intervention results in 50% of increase of condom use and 50 % decrease of needle sharing. The incidence change for a specific population could be the result of several interventions.

D3c. Population Models

Population models look at how the intervention affects the incidence and prevalence of HIV in the community as a whole, over time. Often, these models use differential equations to estimate changes in incidence and prevalence. Again, the difference in the incidence expected with the intervention and without the intervention, coupled with an estimate of the size of the affected population, provides an estimate of the number of infections averted by the intervention.

E0. Limitations of Economic Evaluation Literature

Several limitations of the HIV prevention economic evaluation literature make it difficult to compare across studies, or to directly apply the results of these studies. First, studies may differ in any of a number of ways, such as: (1) the **economic evaluation** technique used (for example, **cost-effectiveness** versus **cost-utility analysis**); (2) the **mathematical models** used to estimate the number of infections averted by the intervention, and in particular, whether they assess the impact of the intervention on the partners of intervention participants or the population as a whole; (3) the values of key epidemiological parameters used in the **mathematical models**; (4) the quality and suitability of the behavioral data collected in the intervention trial; and (5) the specific framework and assumptions underlying the **cost analysis** (e.g., costs might be reported in different base-year dollars, different discount rates might be used, or different **perspectives** might been adopted for the analyses).

A second important limitation of these analyses is that the results cannot easily be generalized from one population group to another, or from one geographical or environmental context to another. The number of infections averted by an intervention depends on the behavioral risk levels of the clients both before and after the intervention; the prevalence of HIV infection among their sex and needle-sharing partners; and the number of people reached by the intervention. The same intervention, implemented in two different contexts or with two different populations, might have very different consequences in terms of the number of infections averted.

The existing literature also suffers from a form of **selection bias**. That is, only a very select subgroup of potential HIV prevention interventions have been evaluated to date. This does not mean that these are the only cost-effective interventions, only that they are the only ones whose cost-effectiveness has been assessed.

Finally, consumers of the economic evaluation literature must be aware that these studies are not intended as accounting studies, and therefore some imprecision in cost estimates is to be expected. Likewise, it is not possible to determine the exact number of infections averted by an intervention. The models that are used to estimate the number of infections averted are constrained by the behavioral data that are collected during intervention evaluation studies and necessarily make many simplifying assumptions. They also must rely on imperfect estimates of epidemiological parameters such as the per-act probability of HIV transmission, the effectiveness of condoms in preventing transmission, the prevalence of infection in the population, and so forth. As a consequence, some degree of imprecision is unavoidable.

Annotated Bibliography

A very good introductory book on applying **economic evaluation** techniques to preventive services is:

Haddix, A.C., Teutsch, S.M., Shaffer, P.A, & Duñet, D.O. (1996). Prevention Effectiveness: A Guide to Decision Analysis and Economic Evaluation. New York: Oxford University Press.

A more comprehensive, but rather technical discussion of specific issues involved in evaluating the cost-effectiveness of health-related interventions is provided by:

Gold, M.R., Siegel, J.E., Russell, L.B., & Weinstein, M.C. (Eds.) (1996). Cost-effectiveness in Health and Medicine. New York: Oxford University Press.

The following journal articles and book chapter describe how cost-effectiveness techniques can be applied to HIV prevention interventions:

Kahn, J.G., & Haynes-Sanstad, K.C. (1997). The role of cost-effectiveness analysis in assessing HIV-prevention interventions. AIDS & Public Policy Journal, 12, 21-30.

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Two of the most comprehensive reviews of the literature on the cost-effectiveness of sexual risk reduction HIV prevention interventions are listed below. The first of these articles provides summary descriptions of the target interventions and qualitative overviews of the cost-effectiveness findings, whereas the second provides a more quantitative review.

Pinkerton, S.D., Johnson-Masotti, A.P., Holtgrave, D.R., & Farnham, P.G. (2002). A review of the cost-effectiveness of interventions to prevent sexual transmission of HIV in the United States. AIDS and Behavior, 6, 15-31.

Pinkerton, S.D., Johnson-Masotti, A.P., Holtgrave, D.R., & Farnham, P.G. (2001). Using cost-effectiveness league tables to compare interventions to prevent sexual transmission of HIV. AIDS, 15, 917-928.

Two recent articles summarize methods for prioritizing interventions and decision making in the context of HIV prevention community planning:

Johnson-Masotti, A.P., Pinkerton, S.D., & Holtgrave, D.R. (2000). Prioritization methods for HIV community planning. Journal of Public Health Management and Practice, 6, 72-85.

Johnson-Masotti, A.P., Pinkerton, S.D., Holtgrave, D.R., Valdiserri, R.O., & Willingham, M. (2000). Decision-making in HIV prevention community planning: an integrative review. Journal of Community Health, 25, 95-112.

Good discussions of HIV prevention **resource allocation** and some of the difficulties faced in this process can be found in:

Paltiel, A.D., & Stinnett, A.A. (1998). Resource allocation and the funding of HIV prevention. In D.R. Holtgrave (ed.), Handbook of Economic Evaluation of HIV Prevention Programs (pp. 135-152). New York: Plenum Press.

Weinstein, B., & Melchreit, R.L. (1998). Economic evaluation and HIV prevention decision making. In D.R. Holtgrave (ed.), Handbook of Economic Evaluation of HIV Prevention Programs (pp. 153-162). New York: Plenum Press.

David Holtgrave's edited volume is a good resource for learning more about HIV prevention economic evaluation techniques, findings from the literature, and different perspectives on the role of economics in HIV prevention:

Holtgrave, D.R. (Ed.) (1998). Handbook of Economic Evaluation of HIV Prevention Programs. New York: Plenum Press.

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